REMARKS

The amendments above serve to define the invention using variables "M" and "L^1" consistent with other copending applications. Other amendments have bees made to differentiate each side of the urea functional group. Only the amendment to the element "L^1"discussed below, has been made to distinguish the reference WO 97/17328.

Rejection Under 35 USC §103

The substituent L^1, an element within all of the compounds claimed, has been limited by the above amendments and does not encompass 6,7- dialkoxy -4-quinoline or 6,7-dialkoxy-4-quinazoline in that where $L^1$is benzopyridine, it can optionally have only have one alkoxy substituent. The structures for Group B of formula I encompass quinoline and quinazoline, however, these structures are directly bound to a urea group, which is not shown in the general formula of WO 97/17329. In compound claims 1-14, the group corresponding to Group A of formula I can be phenyl or naphthyl. The compounds now defined by claims 1-14 are structurally distinct from the compounds generically disclosed by WO 97/17329 and so they are not obvious in view of W0 97/17329.

The method claims have not been amended to limit L^1 of the compounds used with respect to alkoxy substitution on quinoline and quinazoline in that the abstract of WO 97/17329 does not suggest the compounds of this invention are effective raf kinase inhibitors.

In that the neither compounds nor the methods of this invention are suggested by this reference, withdrawal of the rejection under 35 USC §103 based on this reference is appropriate.

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Based on the above remarks, Applicants respectfully request withdrawal of the rejection based on WO 97/017329 and expansion of the examined subject matter to the full scope of the claims. Consideration of the Information Disclosure Statement submitted on December 30, 2002, is also requested.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

Richard J. Traverso (Reg. No. 30,595)
Attorney/Agent for Applicant(s)

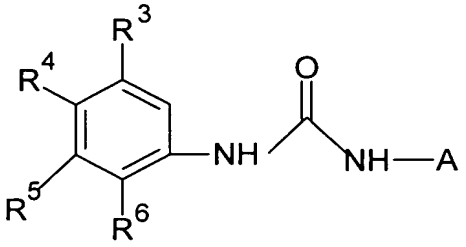
MILLEN, WHITE, ZELANO
& BRANIGAN, P.C.
Arlington Courthouse Plaza 1, Suite 1400
2200 Clarendon Boulevard
Arlington, Virginia 22201
Telephone: (703) 243-6333
Facsimile: (703) 243-6410

Attorney Docket No.: **BAYER 6 P1**

Date: **March 13, 2003**

VERSION WITH MARKINGS TO SHOW THE CHANGES MADE

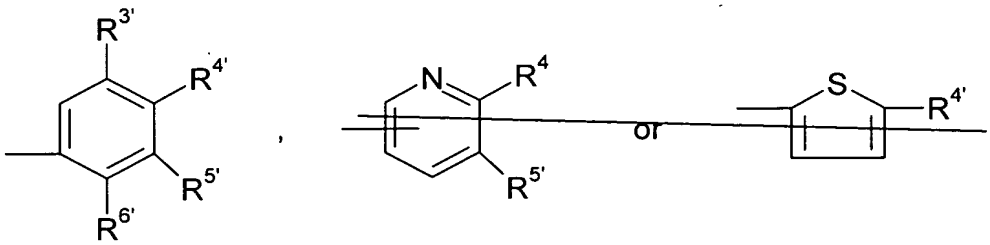
1. (Amended) A compound of formula I:



I

wherein

A is



R^3, R^4 , R^5 and R^6 are each, independently, H, halogen, NO_2, C_{1-10}- alkyl, optionally substituted by halogen up to perhaloalkyl, C_{1-10}-alkoxy, optionally substituted by halogen up to perhaloalkoxy, **C_{1-10}- alkanoyl, optionally substituted by halogen up to perhaloalkanoyl,**

C_{6-12} aryl, optionally substituted by C_{1-10} alkyl or C_{1-10} alkoxy, or C_{5-12} hetaryl, optionally substituted by C_{1-10} alkyl or C_{1-10} alkoxy,

and **either** one of R3-~~**R^6 can be X-Y**~~ **R^3, R4, R^5 and R^6 is –M-L^1**;

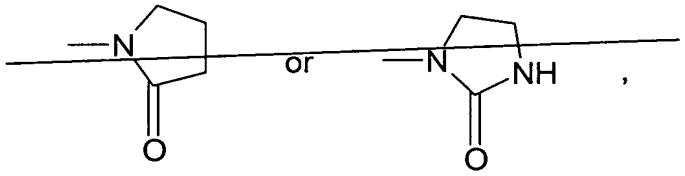
or two adjacent ~~**R^3-R^6 can together be**~~ **of R^3, R^4 , R^5 and R^6 together are** an aryl or hetaryl ring with 5-12 atoms, optionally substituted by C_{1-10}-alkyl, , **halo-substituted C_{1-10}-alkyl up to**

perhaloalkyl, C_{1-10}-alkoxy, **halo-substituted C_{1-10}-alkoxy, up to perhaloalkoxy,** C_{3-10}-cycloalkyl, C_{2-10}-alkenyl,

C_{1-10}-alkanoyl, C_{6-12}-aryl, C_{5-12}-hetaryl; C_{6-12}-aralkyl, C_{6-12}-alkaryl, halogen; NR^1R^1;

$-NO_2$; $-CF_3$; $-COOR^1$; $-NHCOR^1$; -CN; $-CONR^1R^1$; $-SO_2R^2$; $-SOR^2$; $-SR^2$; in which R^1 is H or C_{1-10}-alkyl**, optionally substituted by halogen up to perhaloalkyl** and R^2 is C_{1-10}-alkyl, optionally substituted by halogen, up to **perhaloalkyl**, ~~**perhalo with $S(O_2)$ optionally incorporated in the aryl or hetaryl ring;**~~

$R^{3'}$, $R^{4'}$, $R^{5'}$ and $R^{6'}$ are independently H, halogen, C_1 - C_{10} alkyl, optionally substituted by halogen up to perhaloalkyl,



C_1 –C_{10} alkoxy optionally substituted by halogen up to perhaloalkoxy ~~**or –X-Y, and either one of $R^{4'}$, $R^{5'}$ or $R^{6'}$ is –X-Y**~~ or two adjacent of **$R^{3'}$,** $R^{4'}$, $R^{5'}$ and $R^{6'}$, **together with the base phenyl, form a naphthyl group,** ~~**are a hetaryl ring with 5-12 atoms**~~ optionally substituted by **halogen up to perhalo,** C_{1-10} alkyl, C_{1-10} alkoxy, C_{3-10} cycloalkyl, C_{2-10} alkenyl, C_{1-10} alkanoyl, C_{6-12} aryl, C_{5-12} hetaryl or C_{6-12} aralkyl;

~~$R^{6'}$ is additionally $NHCOR^1$, NR^1COR^1 or NO_2;~~

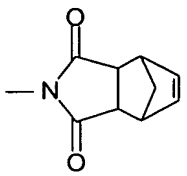
~~R^1 is C_{1-10}-alkyl optionally substituted by halogen up to perhalo;~~

~~$R^{3'}$ is H, halogen, C_1-C_{10}-alkyl optionally substituted by halogen up to perhaloalkyl, C_1-C_{10} alkoxy, optionally substituted by halogen up to perhaloalkoxy~~;

~~X~~ **M** is $–CH_2$-, -S-, $-N(CH_3)$-, -NHC(O)- $-CH_2$-S-, $-S-CH_2$-, -C(O)-, or –O-; and

~~X is additionally a single bond where Y is pyridyl; and~~

~~Y~~ L^1 is phenyl, **optionally substituted by C_{1-10}-alkyl, C_{1-10}-alkoxy, halogen, OH, - SCH_3, NO_2 or,**



pyridyl, **optionally substituted by C_{1-10}-alkyl, C_{1-10}-alkoxy, halogen, OH, -SCH_3, or NO_2,**

naphthyl, **optionally substituted by C_{1-10}-alkyl, C_{1-10}-alkoxy, halogen, OH, -SCH_3 or NO_2,**

pyridone, **optionally substituted by C_{1-10}-alkyl, C_{1-10}-alkoxy, halogen, OH, -SCH_3 or NO_2,**

pyrazine, **optionally substituted by C_{1-10}-alkyl, C_{1-10}-alkoxy, halogen, OH, -SCH_3 or NO_2,**

pyrimidine, **optionally substituted by C_{1-10}-alkyl, C_{1-10}-alkoxy, halogen, OH,**

-SCH_3 or NO_2,

~~benzodiaxane~~ **benzodioxane, optionally substituted by C_{1-10}-alkyl, C_{1-10}-alkoxy, halogen, OH,**

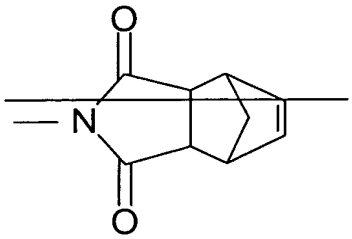
-SCH_3 or NO_2,

benzopyridine, **optionally substituted by C_{1-10}-alkyl, one C_{1-10}-alkoxy, halogen, OH,**

-SCH_3 or NO_2 or

benzothiazole, [~~each~~] optionally substituted by, C_{1-10} alkyl C_{1-10} alkoxy, halogen, OH, -SCH_3 **or** , NO_2; [~~(or, where Y is phenyl~~ by

B



or a pharmaceutically acceptable salt thereof~~,~~

~~with the proviso that if X is –O– or –S–, $R^{3'}$ and $R^{6'}$ are H, and Y is phenyl unsubstituted by OH, then R^6 is alkoxy~~.

2. (Amended) A compound according to claim 1, having a pKa greater than 10.

3. (Amended) A compound according to claim 1, wherein

R^3 is H, halogen or C_{1-10}- alkyl, optionally substituted by halogen, up to perhaloalkyl;

R^4 is H, halogen or NO_2;

R^5 is H, halogen or C_{1-10}- alkyl;

R^6 is H, C_{1-10}- alkoxy, thiophene, pyrole or methyl substituted pyrole,

$R^{3'}$ is H, halogen, **C_{4-10}-alkyl,** ~~CH_3~~, or CF_3 and

$R^{6'}$ is H, halogen CH_3, CF_3 or $-OCH_3$.

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4. (Amended) A compound according to claim 1, wherein

~~R³~~ R^3' is C_{4-10}-alkyl, Cl, F or CF_3;

~~R⁴~~ R^4' is H, Cl or F ~~or NO_2~~;

~~R⁵~~ R^5' is H, Cl, F or C_{4-10}-alkyl; and

~~R⁶~~ R^6' is H or OCH_3.

5. (Amended) A compound according to claim 4, wherein ~~R³~~ R^3' or ~~R⁵~~ R^5' is t-butyl.

6. (Amended) A compound according to claim 1, wherein ~~X~~ M is $-CH_2-$, $-N(CH_3)-$ or –NHC(O)-.

7. (Amended) A compound according to claim 6, wherein ~~Y~~ L^1 is phenyl or pyridyl.

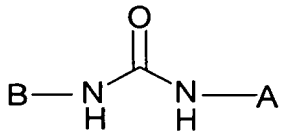
8. (Amended) A compound according to claim 1, wherein ~~X~~ M is –O-.

9. (Amended) A compound according to claim 8, wherein ~~Y~~ L^1 is phenyl, pyridyl pyridone or benzothiazole.

10. (Amended) A compound according to claim 1, wherein ~~X~~ M- is –S-.

11. (Amended) A compound according to claim 10, wherein ~~Y~~ L^1 is phenyl or pyridyl.

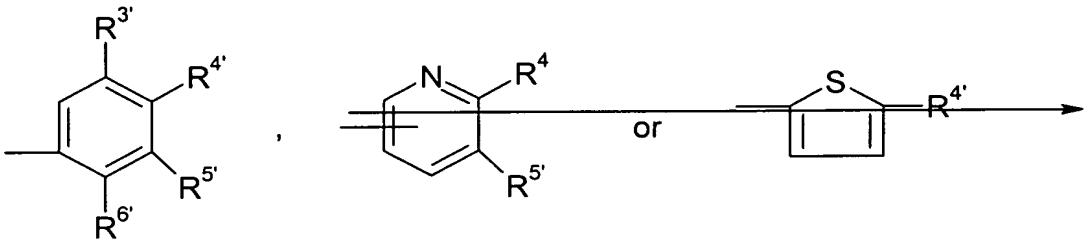
15. (Amended) A method for the treatment of a cancerous cell growth mediated by raf kinase, comprising administering a compound of formula II:



II

or a pharmaceutically acceptable salt thereof wherein

A is



B is a substituted or unsubstituted, up to ~~tricyclic~~ bicyclic aryl or heteroaryl moiety of up to ~~30~~ 12 carbon atoms with at least one 6-member aromatic structure containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur, wherein if B is substituted it is substituted by one or more substituents selected from the group consisting of halogen, up to per-halo, and W_n, wherein n is 0-3 and each W is independently selected from the group consisting of –CN, $-CO_2R^7$, $-C(O)NR^7R^7$, $-C(O)-R^7$, $-NO_2$, $-OR^7$, $-SR^7$, $-NR^7R^7$, $-NR^7C(O)OR^7$, $-NR^7C(O)R^7$, C_1-C_{10} alkyl, C_2-C_{10} alkenyl, C_1-C_{10} alkenoyl, C_1-C_{10} alkoxy, C_3-C_{10} cycloalkyl, C_6-C_{14} aryl, optionally substituted with halogen, C_1-C_{10} alkyl, or C_1-C_{10} alkoxy; C_7-C_{24} alkaryl, optionally substituted with halogen, C_1-C_{10} alkyl, or C_1-C_{10} alkoxy; C_3-C_{13} heteroaryl, optionally substituted with halogen, C_1-C_{10} alkyl, or C_1-C_{10} alkoxy; C_4-C_{23} alkheteroaryl, optionally substituted with halogen, C_1-C_{10} alkyl, or C_1-C_{10} alkoxy; substituted C_1-C_{10} alkyl, substituted C_2-C_{10} alkenyl, substituted C_1-C_{10} alkenoyl, substituted C_1-C_{10} alkoxy, substituted C_3-C_{10} cycloalkyl, substituted C_4-C_{23} alkheteroaryl and –M-L^1 ~~Q-Ar~~;

wherein if W is a substituted group which does not contain aryl or hetaryl moieties, it is substituted by one or more substituents independently selected from the group consisting of –CN, $-CO_2R^7$, $-C(O)R^7$, $-C(O)NR^7R^7$, $-OR^7$, $-SR^7$, $-NR^7R^7$, NO_2, $-NR^7C(O)R^7$, $-NR^7C(O)OR^7$ and halogen up to per-halo;

wherein each R^7 is independently selected from H, C_1-C_{10} alkyl, C_2-C_{10} alkenyl, C_3-C_{10}

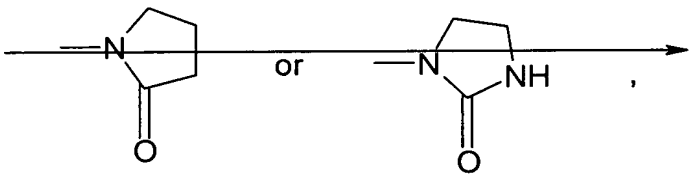
cycloalkyl, C_6-C_{14} aryl, C_3-C_{13} hetaryl, C_7-C_{24} alkaryl, C_4-C_{23} alkheteroaryl, up to per-halosubstituted C_1-C_{10} alkyl, up to per-halo substituted C_2-C_{10} alkenyl, up to per-halosubstituted C_3-C_{10} cycloalkyl, up to per-halosubstituted C_6-C_{14} aryl and up to per-halosubstituted C_3-C_{13} hetaryl,

wherein ~~Q~~ M is - O-, -S-, -N(R^7)-, -$(CH_2)_{-m}$, -C(O)-, -CH(OH)-, -$(CH_2)_m$O-, -$NR^7C(O)$ NR^7R^7-, -$NR^7C(O)$-, -$C(O)NR^7$-, -$(CH_2)_m$S-, -$(CH_2)_m$N(R^7)-, -$O(CH_2)_m$-, -CHX^a, -CX^a_2-, -S-$(CH_2)_m$- and -N(R^7)$(CH_2)_m$-,

m = 1-3, and X^a is halogen; and

~~Ar~~ L^1 is a 5-10 member aromatic structure containing 0-2 members of the group consisting of nitrogen, oxygen and sulfur, which is unsubstituted or substituted by halogen up to per-halo and optionally substituted by Z_{n1}, wherein $n1$ is 0 to 3 and each Z is independently selected from the group consisting of –CN, -CO_2R^7, -$C(O)NR^7R^7$, -C(O)- NR^7, -NO_2, -OR^7, - SR^7, - NR^7R^7, -$NR^7C(O)OR^7$, -$C(O)R^7$, -$NR^7C(O)R^7$, C_1-C_{10} alkyl, C_3-C_{10} cycloalkyl, C_6-C_{14} aryl, C_3-C_{13} hetaryl, C_7-C_{24} alkaryl, C_4-C_{23} alkheteroaryl, substituted C_1-C_{10} alkyl, substituted C_3-C_{10} cycloalkyl, substituted C_7-C_{24} alkaryl and substituted C_4-C_{23} alkheteroaryl; wherein the one or more substituents of Z is selected from the group consisting of –CN, -CO_2R^7, -$C(O)NR^7R^7$, -OR^7, -SR^7, -NO_2, -NR^7R^7 , -$NR^7C(O)R^7$ and -$NR^7C(O)OR^7$,

wherein $R^{3'}$, $R^{4'}$,$R^{5'}$and $R^{6'}$ are each independently H, halogen, C_{1-10}-alkyl, optionally substituted by halogen up to perhaloalkyl,



C_1 –C_{10} alkoxy, optionally substituted by halogen up to perhaloalkoxy or ~~–X-Y,~~ ~~and~~

~~either one of $R^{4'}$, $R^{5'}$ or $R^{6'}$ is –X-Y- or~~ two adjacent of $R^{3'}$,$R^{4'}$, $R^{5'}$ and $R^{6'}$ together with the base phenyl, form a naphthyl group~~, are a hetaryl ring with 5-12 atoms~~ optionally

substituted by halogen up to perhalo, C_{1-10} alkyl, C_{1-10} alkoxy, C_{3-10} cycloalkyl, C_{2-10} alkenyl, C_{1-10} alkanoyl, C_{6-12} aryl, C_{5-12} hetaryl or C_{6-12} aralkyl;

~~$R^{6'}$ is additionally $NHCOR^1$, NR^1COR^1 or NO_2;~~

~~R^1 is C_{1-10} alkyl optionally substituted by halogen up to perhalo;~~

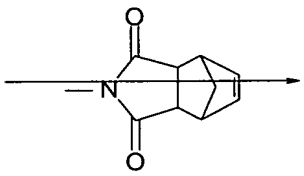
~~$R^{3'}$ is independently H, halogen, C_{1-10} alkyl, optionally substituted by halogen up to perhaloalkyl, C_{1-10} alkoxy, optionally substituted by halogen up to perhaloalkoxy;~~

~~X is CH_2, S, $N(CH_3)$, NHC(O), CH_2S, C(O), or O;~~

~~X is additionally a single bond where Y is pyridyl; and~~

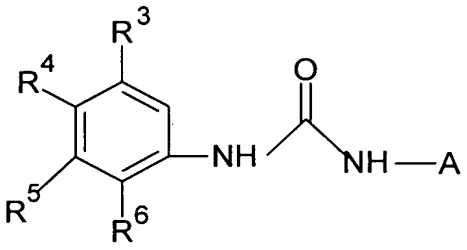
~~Y is phenyl, pyridyl, naphthyl, pyridone, pyrazine, pyrimidine, benzodioxane, benzopyridine or benzothiazole, each optionally substituted by~~

~~C_{1-10} alkyl, C_{1-10} alkoxy, halogen, OH, SCH_3, or NO_2 or, where Y is phenyl, by~~



~~or a pharmaceutically acceptable salt thereof.~~

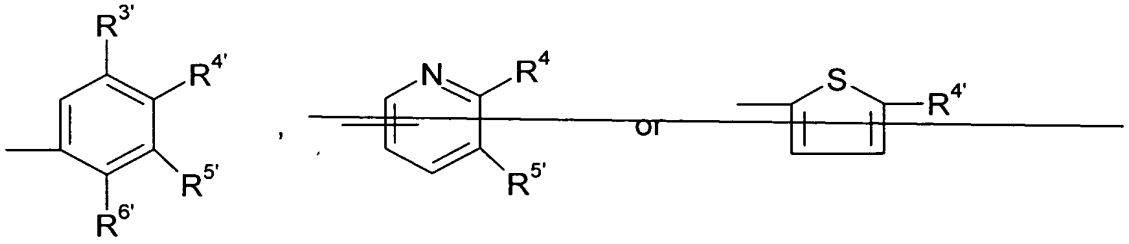
16. (Amended) A method **for the treatment of a cancerous cell growth mediated by raf kinase,** ~~according to claim 15,~~ comprising administering a compound of formula IIa:



IIa

wherein

A is



R^3, R^4 ,R^5 and R^6 are each independently H, halogen, NO_2, C_{1-10}- alkyl, optionally substituted by halogen up to perhaloalkyl, or C_{1-10}-alkoxy, optionally substituted by halogen up to perhaloalkoxy, , **C_{1-10}- alkanoyl, optionally substituted by halogen up to perhaloalkanoyl,** C_{6-12} aryl, optionally substituted by C_{1-10} alkyl or C_{1-10} alkoxy, or C_{5-12} hetaryl, optionally substituted by C_{1-10} alkyl or C_{1-10} alkoxy,

and **either** one of ~~R^3-R^6 can be X-Y~~ **R^3, R^4 , R^5 and R^6 is –M-L^1**;

or two adjacent ~~R^3 R^6 can together be~~ **of R^3, R^4, R^5 and R^6 together are** an aryl or hetaryl ring with 5-12 atoms, optionally substituted by C_{1-10}-alkyl, **halo-substituted C_{1-10}-alkyl up to perhaloalkyl**, C_{1-10}-alkoxy, **halo-substituted C_{1-10}-alkoxy, up to perhaloalkoxy,** C_{3-10}-cycloalkyl, C_{2-10}-alkenyl,

C_{1-10}-alkanoyl; C_{6-12}-aryl, C_{5-12}-hetaryl, C_{6-12}-alkaryl, halogen; $-NR^1R^1$; $-NO_2$; $-CF_3$; $-COOR^1$; $-NHCOR^1$; -CN; $-CONR^1R^1$; $-SO_2R^2$; $-SOR^2$; $-SR^2$; in which R^1 is H or C_{1-10}-alkyl, optionally substituted by halogen, up to perhalo and R^2 is C_{1-10}-alkyl, optionally substituted by halogen, ~~up to perhalo, with $-SO_2-$ optionally incorporated in the aryl or hetaryl ring, and $R^{3'}$ - $R^{6'}$ are as defined in claim 15.~~

$R^{3'}$, $R^{4'}$, $R^{5'}$ and $R^{6'}$ are independently H, halogen, C_1 - C_{10} alkyl, optionally substituted by halogen up to perhaloalkyl,

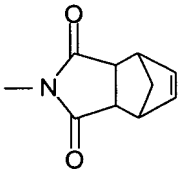
C_1 –C_{10} alkoxy optionally substituted by halogen up to perhaloalkoxy or two adjacent of $R^{3'}$, $R^{4'}$, $R^{5'}$ and $R^{6'}$, together with the base phenyl, form a naphthyl group optionally substituted by halogen up to perhalo, C_{1-10} alkyl, C_{1-10} alkoxy, C_{3-10} cycloalkyl, C_{2-10} alkenyl, C_{1-10} alkanoyl,

C_{6-12} aryl, C_{5-12} hetaryl or C_{6-12} aralkyl, halogen up to perhalo ;

R^1 is C_{1-10} alkyl optionally substituted by halogen up to perhalo;

M is $-CH_2-$, -S-, $-N(CH_3)-$, -NHC(O)- $-CH_2-S-$, $-S-CH_2-$, -C(O)-, or –O-; and

L^1 is phenyl, pyridyl, naphthyl, pyridone, pyrazine, pyrimidine, benzodiaxane, benzopyridine or benzothiazole, each optionally substituted by C_{1-10}-alkyl, C_{1-10}-alkoxy, halogen, OH, $-SCH_3$, NO_2 or, where Y is phenyl, by



or a pharmaceutically acceptable salt thereof.

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17. A method according to claim 16, wherein

R^3 is halogen or C_{1-10}- alkyl, optionally substituted by halogen, up to perhaloalkyl;

R^4 is H, halogen or NO_2;

R^5 is H, halogen or C_{1-10}- alkyl;

R^6 is H [or] C_{1-10}- alkoxy, thiophene, pyrole or methylsubstituted pyrole

$R^{3'}$ is H, halogen, **C_{4-10}-alkyl,** ~~CH_3~~, or CF_3 and

$R^{6'}$ is H, halogen, CH_3 , CF_3 or OCH_3.

18. A method according to claim 16, wherein ~~X~~ **M** is $-CH_2-$, ~~or~~ –S-, $-N(CH_3)-$ or –NHC(O)- and ~~Y~~ L^1 is phenyl or pyridyl.

19. A method according to claim 16, wherein ~~X~~ **M** is –O- and ~~Y~~ L^1 is phenyl, pyridone, pyrimidine, pyridyl or benzothiazole.

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